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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,864	03/30/2006	Wen-Luan Wendy Hsiao	32144183.4	8549
51738	7590	04/28/2008		
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HOUSTON, TX 77002-2716			ART UNIT	PAPER NUMBER
			1634	
			MAIL DATE	DELIVERY MODE
			04/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/516,864	<b>Applicant(s)</b> HSIAO ET AL.
	<b>Examiner</b> JEANINE A. GOLDBERG	<b>Art Unit</b> 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 15 January 2008.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-29 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date: _____          |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application<br>Paper No(s)/Mail Date _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____   |

**DETAILED ACTION**

1. This action is in response to the papers filed January 15, 2008. Currently, claims 1-29 are pending.
2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.
3. Any objections and rejections not reiterated below are hereby withdrawn.

***Maintained Rejections***

***Election/Restrictions***

4. Applicant's election with traverse of Group 1, Claims 1-29 directed to gene-encoded beta-catenin in the paper filed August 6, 2007 is acknowledged.

The response asserts that the practice regarding nucleotide sequences permits examination of up to ten sequences as set forth in the 1996 OG notice.

An OG Notice published March 27, 2007 rescinded the 1996 OG Notice that provided for a partial waiver of the requirements for restriction practice by permitting examination of a reasonable number, up to ten, independent and distinct polynucleotide molecules in a single 35 USC 111(a) or 35 USC 371 application. The Notice indicated that the standard of independence and distinctness would be applied to polynucleotide claims filed in an application under 35 USC 111(a). Additionally, the March 27, 2007 OG Notice specifically spoke to the issue of burden of searching more than one independent and distinct invention.

Applicant was provided an opportunity to specifically state on the record that the species were not patentably distinct. "Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention." Applicants do not appear to have availed them of this opportunity.

The response asserts that election of species practice requires that the examiner must examine all members of the Markush group if the search may be made without serious burden. The response asserts that examination of a gene-encoded beta catenin; a gene-encoded alpha-catenin; and a gene encoded E-cadherin would not place undue burden upon the examiner. This argument has been reviewed but is not considered persuasive because each of these genes encode distinct proteins. Although the applicant asserts that the genes are associated, the genes would require a separate search and examination.

The requirement is still deemed proper and is therefore made FINAL.

***Priority***

5. This application is a 371 of PCT/US03/20587, filed June 27, 2003 and provisional application 60/392,191, filed June 28, 2002.

***Drawings***

6. The correction to the drawings has been reviewed. Drawing pages 4-5 have been cancelled as requested by applicant.

***Information Disclosure Statement***

7. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Pages 16-17 contains a list of references. Any references appear in the list and not listed on the IDS have not been considered.

***Claim Objections***

8. Claim 4, 9, 25 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 requires

beta-catenin and Claim 4 appears to further limit the beta-catenin RNA by changing the gene. This does not further limit the subject matter. Similarly, Claims 9, 14, 19, and 25 are drafted like Claim 4.

### **Response**

The response does not appear to address the object. It is noted that Claim 4 remains drawn to a DNA derived from beta-catenin. It is unclear whether the claim further limits Claim 1. Claim 1 requires beta-catenin. Thus, it would appear that a gene derived from beta-catenin would be broader than just the beta-catenin gene. Thus for the reasons above and those already of record, the rejection is maintained.

9. Newly amended Claims 2, 7, 23 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 requires detecting colorectal carcinoma. Claim 2 appear to further limit the carcinoma to colorectal cancer. This does not appear to further limit Claim 2. Similarly, Claims 7 and 23 are drafted like Claim 2.

### ***Claim Rejections - 35 USC § 112- Enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

The claims are broadly drawn to a method for detecting colorectal carcinoma in any patient by extracting blood serum or plasma and detecting the presence or absence of beta-catenin to determine the presence of cancer based on the detected presence of beta-catenin nucleic acid.

The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

Adenomas are benign epithelial tumors arising in epithelium of mucosa (stomach, small intestine and bowel), glands (endocrine and exocrine) and ducts. Thus, Adenomas are not cancer.

The art (Wong et al. Clinical Cancer Research, Vol. 10, pages 1613-1617, March 2004) teaches the quantification of plasma b-catenin mRNA in colorectal cancer and adenoma patients. Wong teaches detecting mRNA in plasma in colorectal carcinoma, colorectal adenoma and normal subjects. The results are listed below.

Carcinoma	1480-933100
Adenoma	541-2254
Normal	0-1366

Wong teaches that b-catenin mRNA was detected in the plasma of all 58 colorectal cancer patients; 49 colorectal adenoma patients and 36 or 43 (84%) of normal subjects. Thus, the majority of normal patients express b-catenin mRNA in the plasma. Figure 1A illustrates the overlapping ranges of mRNA copies in plasma. Wong states that a more intensive study is necessary to explore whether plasma b-catenin mRNA concentration may be a prognostic factor. Wong further proposes that a large-scale study would be needed to investigate whether plasma b-catenin mRNA might have a role in population screening for colorectal cancer (page 1616, col. 2).

Osman et al (Clin Cancer, Res. Vol. 12, No. 11, pages 3374-3380, June 2006) teaches analysis of biomarkers in the blood for various cancers. Osman teaches testing a hypothesis that blood cell gene expression can differentiate between different cancers as well as between controls. Osman teaches concludes the gene expression patterns

found in bladder cancer was distinguishable from other cancers. Thus, Osman teaches an expression pattern for one gene in the blood is not indicative of any cancer.

Fleischhacker et al. (*Biochimica et Biophysica Acta*, Vol. 1775, pages 181-232, 2007) provides a review of circulating nucleic acids (CNAs) and cancer. Fleischhacker teaches that contradictory results have been published between the detection of free-circulating plasma mRNA and clinical data (page 214, col. 2). Fleischhacker teaches the DNA yield from serum is higher than that from plasma (page 219, col. 1).

Guidance in the Specification.

The specification teaches analysis of plasma RNA in carcinoma, adenomas and normal individuals. The results showed that 100% of patients with carcinoma, 11/14 patients with adenoma and 1/10 healthy volunteers carried b-catenin RNA (page 6, lines 19-25). The specification further teaches a quantitative analysis of plasma blood B-catenin RNA. The specification teaches the adenoma b-catenin mRNA was 30 fold higher than in normal individuals.

Carcinoma	6700-44000
Adenoma	690-1800
Normal	0-169

The specification further teaches detection of b-catenin DNA in serum of patients with colorectal adenoma and carcinoma. The specification teaches that serum B-catenin DNA is detectable in all patients with colorectal carcinoma and 9/10 patients with

colorectal adenoma, while all 10 healthy individuals were free of serum b-catenin DNA (page 9, lines 12-15).

The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

#### Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied.

The claims are broadly drawn to **any patient**, as provided in Claim 5, for example. A patient encompasses humans, dogs, and cats among other animals. The instant specification appears to be limited to humans. There is no analysis of expression levels of beta-catenin in dog plasma and any cancer. While the art teaches that dogs suffer from colorectal cancer, there is no indication or expectation that beta-catenin is found in the circulating plasma or serum of dogs. The skilled artisan would be required to determine that the mechanisms of cells in dogs, like human, have circulating DNA and the circulating DNA is expressed in the same proportions as human CANs. Without further experimentation, the skilled artisan would not be able to apply the instant analysis to any patients.

The claims are directed to detecting the presence or absence of beta-catenin nucleic acid. The skilled artisan would be unable to detecting the presence of b-catenin as a positive indicator of cancer because the results illustrate a normal individual with circulating b-catenin. Moreover the art, which appears to be a larger study clearly illustrates that 84% of normal patients were found to have beta-catenin in the plasma.

Thus, it would be unpredictable whether any individual with b-catenin in the circulating DNA would determine the presence of the cancer. Since the vast majority of normal individuals in the study of Wong had b-catenin nucleic acid, it is unpredictable how the skilled artisan would distinguish those with cancer from those not having cancer.

Claims 11 and 16 are directed to “beta-catenin associated gene DNA”. The response to the restriction requirement asserts that a gene-encoded alpha-catenin; and a gene encoded E-cadherin are associated genes. The instant specification fails to provide any analysis of a gene-encoded alpha-catenin; and a gene encoded E-cadherin and colorectal cancer or any cancer. As noted above, Osman teaches that each gene has different profiles in different cancers and thus would require analysis to confirm the pattern of the expression. The art similarly fails to provide any analysis. With regard to the quantification claims, there is no analysis of the concentration of the “associated” genes and whether the same ranges are applicable.

Claim 22 is drawn to a quantitative method for detecting beta-catenin based upon ratios. Claim 22 encompasses detecting the absence of carcinoma and adenoma in patients. The claim sets out several values for detecting adenoma , carcinoma or absence of carcinoma/adenoma. The specification and the art teaches a limited number of individuals who had no b-catenin in the plasma. Thus, the normal individuals would have a value of “0”. A value of zero in the denominator will not result in a value in any of these ranges, as the value is non-existent. Further, the values provided do not appear to be consistent with the data provided in the art or specification. For example, the median concentration taught in the art for carcinoma patients is 8737. The median value for normal individuals is 291. The ratio would be  $8737/291=30$ . According to the claims, this would be indicative of the presence of adenoma. However, this is carcinoma data.

The concentration taught in the specification for carcinoma patients ranges from 6700-44000 and the range in normal patients is 0-169. The ratio of 6700/169= 39 which is within the range for adenoma. This again provides results inconsistent with the claims. Therefore, the quantitative ratios provided in the claims do not appear to enable any reliable detection of carcinoma, adenoma or absence of carcinoma/adenoma. The skilled artisan would be unable to use the teachings to accurately determine the status of the patient.

Furthermore, Claim 22 is drawn to serum or plasma levels. Fleischhacker teaches the DNA yield from serum is higher than that from plasma (page 219, col. 1). The instant specification only provides quantitative analysis for plasma. There is no indication that the serum and plasma levels are in proportion. Therefore, since the art teaches that the serum and plasma levels are expected to differ. And there are no teachings how these levels for b-catenin differ, the skilled artisan would be required to perform further experimentation which is unpredictable to determine how the ratios in the different populations range. There is no expectation that the ranges will not be overlapping, as the plasma levels are overlapping.

This would require significant inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the art and the specification do not support the claims. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized difficulties in cancer diagnostics in the serum and plasma. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

### **Response to Arguments**

The response traverses the rejection. The response asserts This argument has been considered but is not convincing because the Thus for the reasons above and those already of record, the rejection is maintained.

### **Response to Arguments**

The response traverses the rejection. The response asserts the detection of RNA and DNA are routine in all biochemistry laboratories. The examiner agrees that the detection of RNA and DNA is well established. However, the association of particular DNA and RNA levels or sequences with a particular disease is not routine.

The response individually addresses the references cited. With respect to Wong, the response is correct that Wong is not prior art. Wong however demonstrates the unpredictability in the art related to the levels of B-catenin in plasma and serum as

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indicative of colorectal cancer. The response asserts that the statement from Wong as using plasma b-catenin RNA measurements for screening for colorectal cancer is just one statement. This argument has been reviewed, but not convincing. Wong clearly teaches the analysis, similar to the instant specification, but cautions the use of the data without additional investigations and a large scale study. It does not appear to be contrary to the entire reference as a whole because Wong while noting a potential of plasma B-catenin mRNA as a marker for colorectal cancer patients, suggests additional experimentation is needed prior to using this as a diagnostic screening, as specifically claimed in the instant claims.

Regardless of the authorship of the Wong reference, the Wong reference provides data of overlapping ranges, and data which raises the issue of unpredictability of the art and the enablement of the instant claims.

With respect to the Osmer reference, the reference was used to demonstrate that one gene is generally not enough for a diagnostic without further data and that each gene has different profiles in different cancers and thus would require analysis to confirm the pattern of the expression.

With respect to Fleischhacker, the reference is used to demonstrate the differences in serum and plasma levels, thus demonstrating the unpredictability in levels and ratios between serum and plasma. The level determined for serum would not be analogous to the level of plasma. Thus, the claims specifically requiring levels and ratios are unpredictable. The response appears to agree with this analysis since the

response states "plasma will yield a greater amount of RNA and DNA than serum (see page 12 of the response filed January 15, 2008.

The response asserts that no experimentation is required to detect b-catenin in patient plasma or serum and determining whether the patient has no neoplastic polyps, colorectal adenoma or colorectal carcinoma. This argument has been reviewed but is not persuasive. Wong specifically raises questions of unpredictability. Wong appears to describe a very similar analysis of b-catenin levels in colorectal cancers. However, the ranges of Wong and the instant specification differ. the art, which appears to be a larger study clearly illustrates that 84% of normal patients were found to have beta-catenin in the plasma. Thus, it would be unpredictable whether any individual with b-catenin in the circulating DNA would determine the presence of the cancer. Since the vast majority of normal individuals in the study of Wong had b-catenin nucleic acid, it is unpredictable how the skilled artisan would distinguish those with cancer from those not having cancer.

The response asserts that there is no unpredictable experimentation required to measure serum or plasma RNA in any animal of choice. As noted above, the detection of a gene in serum or plasma is routine. However, the association between the detection and the colorectal cancer is unpredictable. Thus, as noted above, it is unpredictable whether expression differences of b-catenin in various animals is associated with colorectal cancer. The response appears to present arguments without any form of evidence that dogs and cats would have similar expression of b-catenin in plasma and would be indicative of colorectal cancer.

The response asserts that para 30 discusses serum analysis. This argument has been reviewed. Example 5 is directed to serum of patients with colorectal adenoma and carcinoma. The specification however fails to provide any analysis of levels, as required by claims 22. As noted by Fleischhacker, and acknowledged by the response, serum and plasma levels vary. Thus, it is unpredictable the level of the b-catenin in serum without further unpredictable and undue experimentation.

Reading the claims and their plain meaning, indicates that the presence of b-catenin is intended to be indicative of colorectal cancer. As noted in the specification, Wong and the response filed January 15, 2008, low beta-catenin is found in normal patients. Thus, the presence of low levels of beta-catenin would appear to be claim to be indicative of colorectal cancer which is in conflict with the specification, Wong and the response. the claims are not directed to any level or amount, but the mere presence.

The response asserts that no evidence has been provided to contradict the enablement. This argument has been considered but is not convincing because the teachings of Wong, Fleischhacker each suggest that b-catenin is present in normal patients. Moreover, it is clear that serum and plasma levels differ and as such, the ratios would be different and unpredictable.

The response provides a table on page 15 of the ratio range/36. it is noted that 6700/36 is not 185 as represented by the table. Similarly, 44000/36 is 1222 and not 1225. It is unclear where the numbers from the response are derived.

	USSN 10/516,864		Ratio Range / (36)
	Range	Median	
Carcinoma	6700-44000	22000	185-1225
Adenoma	690-1800	1100	20-50
Normal	0-169	<b>36</b>	0-5

If a similar table is constructed for the data from Wong, the ranges of ratios are overlapping.

Wong	
Range	Median
1480-933,100	8737
541-2,254	1218
0-1,366	291

Ratio Range/(291)
5-3206
1.9-7.7
0-4.69

This illustrates the overlapping ratios and ranges and provides evidence of the unpredictable results. In the event that one were to obtain a ratio of 5, looking at applicants data in the specification, the person is deemed normal. However, looking at the data from Wong, a ratio of 5 indicates both adenoma and carcinoma. It is unclear how to determine whether a person is normal or has cancer based upon such a ratio. Looking at the ratio of adenoma, the ratio from Wong is not within any of the ranges from the specification. Thus, it is unpredictable. Similar discrepancies could be noted with the ranges, medians and ratios.

The declaration under 37 CFR 1.132 filed January 15, 2008 is insufficient to overcome the rejection of the claims based upon the unpredictability in the art as set

forth in the last Office action. The declaration appears to be directed only to part of the enablement rejection to clarify the results and provide a figure illustrating the results in para 30 of the specification. The declaration further provides an explanation regarding the authorship of the Wong references, however, this does not appear to be related to the enablement rejection. Finally, the declaration states that beta-catenin is representative of many catenin/cadherins and the expression patterns would be similar. First, the additional species amended to be presented in Claim 1, for example have not been considered for the reasons above in the response to the election of species. Moreover, the arguments provided in the declaration are not in the form of evidence.

Thus for the reasons above and those already of record, the rejection is maintained.

- .
- Claim Rejections - 35 USC § 112- Second Paragraph***
- The following is a quotation of the second paragraph of 35 U.S.C. 112:
- The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
11. Claims 1-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-29 are methods for detecting cancer in a patient by extracting serum or plasma from the patient and detecting beta-catenin. As written the claim is unclear whether the process merely requires detecting beta-catenin in the serum and

plasma or whether the claim requires making the association between the presence of the nucleic acid and cancer. The metes and bounds of the claimed invention is unclear. To overcome the instant rejection, the claim could be easily amended to require that "wherein the presence of beta-catenin RNA is indicative of cancer." Similarly, Claims 6, 11, 16 are rejected.

### **Response to Arguments**

The response traverses the rejection. The response asserts the claims are drafted to require a correlation between the presence of beta catenin and presence of colorectal cancer. This argument has been considered but is not convincing because the claim does not require any particular correlation. As noted above, if applicant wishes to clearly indicate that there is a correlation, the claim could be easily amended to require that "wherein the presence of beta-catenin RNA is indicative of cancer." Thus for the reasons above and those already of record, the rejection is maintained.

B) Newly amended Claim 21 is indefinite because "high levels of beta-catenin" The term "high" in claim 21 is a relative term which renders the claim indefinite. The term "high" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

C) Claims 22-28 recites "approximately above" and "approximately 1". The terms are relative terms which renders the claim indefinite. The terms "approximately above" and "approximately 1" are not defined by the claim, the specification does not

provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

### **Response to Arguments**

The response traverses the rejection. The response asserts "approximately" is defined by the ratio described in the claims and the range of beta-catenin. This argument has been considered but is not convincing because the claims do not provide any particular metes and bounds for approximately. The limitations of a range is not read into the claim. Thus for the reasons above and those already of record, the rejection is maintained.

### ***Conclusion***

12. No claims allowable.
13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

*/Jeanine A Goldberg/  
Primary Examiner, Art Unit 1634  
April 25, 2008*